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September 1, 2005

CERTIFICATE OF MAILING
37 C.F.R. 1.8

I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date below:

September 1, 2005
Date

Monica A. De La Paz

Mail Stop Petition
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Re: *SN 09/599,152 "ETHYLENEDICYSTEINE (EC)-DRUG CONJUGATES, COMPOSITIONS AND METHODS FOR TISSUE SPECIFIC DISEASE IMAGING" by Yang, et al.*
Our Ref. UTXC:664; Client Ref. MDA99-040

Commissioner:

Enclosed for filing in the above-referenced patent application is:

(1) Petition For Reconsideration of Restriction Requirement Under 37 C.F.R. § 1.144; and

(2) A return postcard to acknowledge receipt of these materials. Please date stamp and mail this postcard.

The Commissioner is authorized to deduct any petition fee required by 37 C.F.R. §§ 1.16 to 1.21 from Fulbright & Jaworski Deposit Account No. 50-1212/UTXC:664.

Respectfully submitted,

Monica A. De La Paz
Reg. No. 54,662

MAD/vv
Enclosures

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CERTIFICATE OF MAILING
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September 1, 2005
Date

Monica A. De La Paz

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Yang, et al.

Serial No.: 09/599,152

Filed: June 21, 2000

For: ETHYLENEDICYSTEINE (EC)-DRUG CONJUGATES, COMPOSITIONS AND METHODS FOR TISSUE SPECIFIC DISEASE IMAGING

Group Art Unit: 1619

Examiner: Jones, D.

Atty. Dkt. No.: UTXC:664

PETITION FOR RECONSIDERATION OF RESTRICTION REQUIREMENT UNDER 37 C.F.R. §1.144

Mail Stop Petition
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In accordance with 37 C.F.R. §1.144, Applicants herein submit this Petition from Requirement for Restriction. In accordance with 37 C.F.R. §1.144, the deadline for filing the Petition from Requirement for Restriction is not later than appeal. As of this date, Applicants have not yet filed a Brief on Appeal. Therefore, this request is timely filed. The Commissioner is authorized to deduct any petition fee required by 37 C.F.R. §§ 1.16 to 1.21 from Fulbright & Jaworski Deposit Account No. 50-1212/UTSC:664US.

A. Statement of Facts

A copy of the originally filed claims is attached as Appendix A. Applicants received a Restriction Requirement dated September 27, 2001 (attached as Exhibit 1). The Restriction Requirement set forth 4 groups of claims (see page 2 of Exhibit 1). On October 26, 2001, Applicants submitted a response to the Restriction Requirement (attached as Exhibit 2), in which Applicants elected the Group II invention (*i.e.*, claims 33-41). As part of their response, Applicants further amended claims 2-32 of the Group I invention, to make then applicable to the Group II invention (by putting them into method claim format). On March 19, 2003, Applicants filed a Request for Continued Examination, which included an Amendment of independent claims 33, 35, and 38 to introduce specific targeting ligands found to be patentable in the Office Action dated April 24, 2002.

On March 29, 2004, Applicants submitted an Amendment that included new claims 56-61. These claims, which are the claims at issue in this Petition, recite as follows:

56. A method of synthesizing a radiolabeled ethylenedicysteine derivative for imaging comprising the steps:

a) obtaining a tissue specific ligand;

b) admixing said ligand with ethylenedicysteine (EC) to obtain an EC-tissue specific ligand derivative; and

c) admixing said EC-tissue specific ligand derivative with a radionuclide and a reducing agent to obtain a radionuclide labeled EC-tissue specific ligand derivative, wherein the EC forms an N_2S_2 chelate with the radionuclide.

57. The method of claim 56, wherein the tissue specific ligand is an anticancer agent, a tumor marker, a folate receptor targeting ligand, a tumor apoptotic cell targeting ligand, a tumor hypoxia targeting ligand, glutamate pentapeptide, or glucose mimetic.

58. A method for labeling a tissue specific ligand for imaging, comprising the steps:

a) obtaining a tissue specific ligand;

b) admixing the tissue specific ligand with ethylenedicysteine (EC) to obtain an EC-ligand conjugate; and

c) reacting the conjugate with ^{99m}Tc in the presence of a reducing agent to form an N_2S_2 chelate between the ethylenedicysteine (with or without linker) and the ^{99m}Tc.

59. The method of claim 58, wherein the tissue specific ligand is an anticancer agent, a tumor marker, a folate receptor targeting ligand, a tumor apoptotic cell targeting ligand, a tumor hypoxia targeting ligand, glutamate pentapeptide, or glucose mimetic.

60. A method of imaging a site within a mammalian body comprising the steps of administering an effective diagnostic amount of a composition comprising a ^{99m}Tc labeled ethylenedicysteine-tissue specific ligand conjugate and detecting a radioactive signal from the ^{99m}Tc localized at the site.

61. The method of claim 60, wherein the tissue specific ligand is an anticancer agent, a tumor marker, a folate receptor targeting ligand, a tumor apoptotic cell targeting ligand, a tumor hypoxia targeting ligand, glutamate pentapeptide, or glucose mimetic.

Applicants received a final Office Action, dated June 25, 2004, in which the Examiner indicated that new claims 56-61 are withdrawn from consideration as being directed to a non-elected invention in accordance with 37 C.F.R. 1.142(b) and *MPEP* §821.03. In particular, the

Examiner stated on the record that "[n]ewly submitted claims 56-61 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: in particular, the claims are broader that [sic] the claims previously examined."

Each of the new claims, however, is clearly part of the elected invention. In particular, claim 56, an independent claim, is identical to originally filed claim 33. Claim 57, which depends from claim 56, recites certain specific subgroups of tissue specific ligands. Claim 58, an independent claim, is identical to originally filed claim 35. Claim 59, which depends from claim 58, recites certain specific subgroups of tissue specific ligands. Claim 60, an independent claim, is identical to originally filed claim 38. New claim 61, which depends from claim 60, recites certain specific subgroups of tissue specific ligands. Thus, each of these claims is part of the elected Group II invention.

In Applicants' response to the final Office Action dated June 25, 2004, Applicants traversed the withdrawal of claims 56-61, and requested that the Examiner reconsider the withdrawal of these claims. In particular, Applicants requested that the Examiner state on the record her reasons for considering these claims to be independent and distinct from the invention as originally claimed.

Applicants received a non-final Office Action dated May 20, 2005, wherein the Examiner reiterated that claims 56-61 are withdrawn from consideration as being drawn to a non-elected invention for reasons of record set forth in the Office Action mailed June 25, 2004.

On August 22, 2005, Applicants' representative, Monica De La Paz, telephoned Examiner Jones to discuss the reason for withdrawal of claims 56-61. The Examiner stated that she would contact Applicants' representative once she had an opportunity to review the file. On August 29, 2005, Applicants' representative received a message from the Examiner indicating that claims 56-61 remain withdrawn for the reasons of record set forth in the latest Office Action.

B. Points to be Considered

Applicants herein request that the withdrawal of claims 56-61 be reconsidered. In particular, the Examiner has cited 37 C.F.R. §1.142(b) as supporting the withdrawal of these claims. 37 C.F.R. §1.142(b) recites:

> "Claims to the invention or inventions not elected, if not canceled, are nevertheless withdrawn from further consideration by the Examiner by the election, subject however, to reinstatement in the event the requirement for restriction is withdrawn or overruled."

As set forth above, each of the independent claims at issue (*i.e.*, claims 56, 58, and 60) is ***identical*** to an originally filed claim that is part of the originally elected Group II invention (*i.e.*, claims 33, 35, and 38, respectively). The three dependent claims in this group (*i.e.*, claims 57, 59, and 61), are also members of the group II invention because they depend from originally filed claims that are members of the group II invention, and differ only in the recitation of certain subgroups of tissue specific ligands.

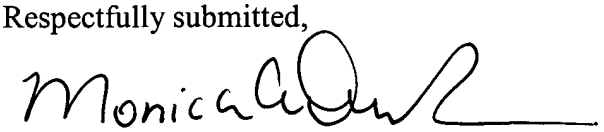
Therefore, the citation of 37 C.F.R. §1.142(b) is inapplicable, because claims 56-61 members of the group of claims elected for further prosecution in response to the original Restriction Requirement.

Nor is the Examiner's citation of *MPEP* §821.03 applicable in supporting the withdrawal of claims 56-61. *MPEP* §821.03 pertains to the disposition of claims for a different invention added after an Office Action. As set forth above, claims 56-61 are drawn to the elected invention, and are thus not directed to a different invention. Therefore, the Examiner's citation of MPEP §821.03 is not relevant and provides no basis for the withdrawal of claims 56-61.

C. Action Requested

WHEREFORE, because claims 56-61 belong to the elected invention, Applicants respectfully request that the Director withdraw the Examiner's withdrawal of these claims and enter these claims into the case.

Respectfully submitted,



Monica A. De La Paz
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Attorney for Applicants

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Date: September 1, 2005

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APPENDIX A

WHAT IS CLAIMED IS:

1. A composition for imaging comprising:

a) a radionuclide label;

b) ethylenedicysteine; and

c) a tissue specific ligand conjugated to said ethylenedicysteine;

wherein said ethylenedicysteine forms an N_2S_2 chelate with said radionuclide label.

2. The composition of claim 1, wherein said tissue specific ligand may be conjugated to said ethylenedicysteine on one or both acid arms of the ethylenedicysteine.

3. The composition of claim 1, wherein said radionuclide is ^{99m}Tc, ^{188}Re, ^{186}Re, ^{183}Sm, ^{166}Ho, ^{90}Y, ^{89}Sr, ^{67}Ga, ^{68}Ga, ^{111}In, ^{183}Gd, ^{59}Fe, ^{225}Ac, ^{212}Bi, ^{211}At, ^{64}Cu or ^{62}Cu.

4. The composition of claim 3, wherein said radionuclide is ^{99m}Tc.

5. The composition of claim 1, wherein said tissue specific ligand is an anticancer agent, DNA topoisomerase inhibitor, antimetabolite, tumor marker, folate receptor targeting ligand, tumor apoptotic cell targeting ligand, tumor hypoxia targeting ligand, DNA intercalator, receptor marker, peptide, nucleotide, organ specific ligand, antibiotic, antifungal, antibody, glutamate pentapeptide or an agent that mimics glucose.

6. The composition of claim 5, wherein said tissue specific ligand is an anticancer agent.

7. The composition of claim 6, wherein said anticancer agent may be selected from the group consisting of methotrexate, doxorubicin, tamoxifen, paclitaxel, topotecan, LHRH, mitomycin C, etoposide tomudex, podophyllotoxin, mitoxantrone, camptothecin, colchicine, endostatin, fludarabin, gemcitabine and tomudex.

8. The composition of claim 5, wherein said tissue specific ligand is a tumor marker.

9. The composition of claim 8, wherein said tumor marker is PSA, ER, PR, CA-125, CA-199, CEA AFP, interferons, BRCA1, HER-2/neu, cytoxan, p53, endostatin or a monoclonal antibody (e.g., antisense).

10. The composition of claim 5, wherein the tissue specific ligand is a folate receptor targeting ligand.

11. The composition of claim 10, wherein the folate receptor targeting ligand is folate, methotrexate or tomudex.

12. The composition of claim 11, further defined as ^{99m}Tc-EC-folate.

13. The composition of claim 11, further defined as ^{99m}Tc-EC-methotrexate.

14. The composition of claim 11, further defined as ^{99m}Tc-EC-tomudex.

15. The composition of claim 5, wherein the tissue specific ligand is a tumor apoptotic cell targeting ligand or a tumor hypoxia targeting ligand.

16. The composition of claim 15, wherein the tissue specific ligand is annexin V, colchicine, nitroimidazole, mitomycin or metronidazole.

17. The composition of claim 16, further defined as ^{99m}Tc-EC-annexin V.

18. The composition of claim 16, further defined as ^{99m}Tc-EC-colchicine.

19. The composition of claim 16, further defined as ^{99m}Tc-EC-nitroimidazole.

20. The composition of claim 16, further defined as ^{99m}TC-EC-metronidas.

21. The composition of claim 5, wherein the tissue specific ligand is glutamate pentapeptide (molecular weight 750-15,000).

22. The composition of claim 21, further defined as 99mTc-EC-glutamate pentapeptide.

23. The composition of claim 5, wherein the tissue specific ligand is an agent that mimics glucose.

24. The composition of claim 23, wherein the agent that mimics glucose is neomycin, kanamycin, getnamycin, paromycin, amikacin, tobramycin, netilmicin, ribostamycin, sisomicin, micromicin, lividomycin, dibekacin, isepamicin, astromicin, or an aminoglycoside.

25. The composition of claim 24, further defined as 99mTc-EC-neomycin.

26. The composition of claim 24, further defined as 99mTc-EC-kanamycin.

27. The composition of claim 24, further defined as 99mTc-EC-aminoglycosides.

28. The composition of claim 24, further defined as 99mTc-EC-gentamycin.

29. The composition of claim 24, further defined as 99mTc-EC-tobramycin.

30. The composition of claim 2, further comprising a linker conjugating EC to said tissue specific ligand.

31. The composition of claim 30, wherein the linker is a water soluble peptide, glutamic acid, aspartic acid, bromo ethylacetate, ethylene diamine or lysine.

32. The composition of claim 31, wherein the tissue specific ligand is estradiol, topotecan, paclitaxel, raloxifen, etoposide, doxorubricin, mitomycin C, endostatin, annexin V, LHRH, octreotide, VIP, methotrexate or folic acid.

33. A method of synthesizing a radiolabeled ethylenedicysteine derivative for imaging comprising the steps:

a) obtaining a tissue specific ligand;

b) admixing said ligand with ethylenedicysteine (EC) to obtain an EC-tissue specific ligand derivative; and

c) admixing said EC-tissue specific ligand derivative with a radionuclide and a reducing agent to obtain a radionuclide labeled EC-tissue specific ligand derivative, wherein the EC forms an N_2S_2 chelate with the radionuclide.

34. The method of claim 33, wherein said reducing agent is a dithionite ion, a stannous ion or a ferrous ion.

35. A method for labeling a tissue specific ligand for imaging, comprising the steps:

a) obtaining a tissue specific ligand;

b) admixing the tissue specific ligand with ethylenedicysteine (EC) to obtain an EC-ligand drug conjugate; and

c) reacting the drug conjugate with ^{99m}Tc in the presence of a reducing agent to form an N_2S_2 chelate between the ethylenedicysteine (with or without linker) and the ^{99m}Tc.

36. The method of claim 35, wherein the tissue specific ligand is an anticancer agent, DNA topoisomerase inhibitor, antimetabolite, tumor marker, folate receptor targeting ligand, tumor apoptotic cell targeting ligand, tumor hypoxia targeting ligand, DNA intercalator, receptor marker, peptide, organ specific ligand, antibiotic, antifungal, glutamate pentapeptide or an agent that mimics glucose.

37. The method of claim 36, wherein the reducing agent is a dithionite ion, a stannous ion or a ferrous ion.

38. A method of imaging a site within a mammalian body comprising the steps of administering an effective diagnostic amount of a composition comprising a 99mTc labeled ethylenedicysteine-tissue specific ligand conjugate and detecting a radioactive signal from the ^{99m}Tc localized at the site.

39. The method of claim 38, wherein the site is a tumor.

40. The method of claim 38, wherein the site is an infection.

41. The method of claim 38, wherein the site is breast cancer, ovarian cancer, prostate cancer, endometrium, heart, lung, brain, liver, folate (+) cancer, ER (+) cancer, spleen, pancreas, or intestine.

42. A kit for preparing a radiopharmaceutical preparation, said kit comprising a sealed container including a predetermined quantity of an ethylenedicysteine-tissue specific ligand conjugate composition and a sufficient amount of reducing agent to label the conjugate with ^{99m}Tc.

43. The kit of claim 42, wherein the ethylenedicysteine-tissue specific ligand conjugate composition further comprises a linker between the ethylenedicysteine and the tissue specific ligand.

44. The kit of claim 42, wherein the tissue specific ligand is an anticancer agent, DNA topoisomerase inhibitor, antimetabolite, tumor marker, folate receptor targeting ligand, tumor apoptotic cell targeting ligand, tumor hypoxia targeting ligand, DNA intercalator, receptor marker, peptide, organ ligand, antibiotic, antifungal, glutamate pentapeptide or an agent that mimics glucose.

45. The kit of claim 43, wherein the tissue specific ligand is estradiol, topotecan, paclitaxel, raloxifen, etoposide, doxorubricin, mitomycin C, endostatin, annexin V, LHRH, octreotide, VIP, methotrexate or folic acid.

46. The kit of claim 45, wherein the linker is a water soluble peptide, glutamic acid, polyglutamic acid, aspartic acid, polyaspartic acid, bromoethylacetate, ethylenediamine or lysine.

47. A reagent for preparing a scintigraphic imaging agent comprising a tissue specific ligand covalently linked to a ^{99m}Tc binding moiety.

48. The reagent of claim 47, wherein the ^{99m}Tc binding moiety is ethylenedicysteine.

49. The reagent of claim 48, wherein the tissue specific ligand is an anticancer agent, DNA topoisomerase inhibitor, antimetabolite, tumor marker, folate receptor targeting ligand, tumor apoptotic cell targeting ligand, tumor hypoxia targeting ligand, DNA intercalator, receptor marker, peptide, organ specific ligand, antibiotic, antifungal, glutamate pentapeptide or an agent that mimics glucose.

50. The reagent of claim 48, further comprising a linker between said tissue specific ligand and said ^{99m}Tc binding moiety.

51. A method of determining effectiveness of a candidate drug on a tumor, said method comprising:

a) obtaining a candidate drug;

b) conjugating said candidate drug with ethylenedicysteine (EC) to produce an EC-candidate drug conjugate;

c) chelating said candidate drug conjugate with ^{99m}Tc to produce a ^{99m}Tc-EC-candidate drug conjugate;

d) introducing said ^{99m}Tc-EC-candidate drug conjugate into a patient with a tumor; and

e) imaging said patient to determine the effectiveness of the candidate drug against the tumor.

EXHIBIT 1

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UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/599,152	06/21/00	YANG	D UTXC:664

HM12/0927

TERESA J BOWLES
600 CONGRESS AVENUE
SUITE 2400
AUSTIN TX 78701

EXAMINER	
JONES, D	
ART UNIT	PAPER NUMBER
1619	8

DATE MAILED: 09/27/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

RECEIVED
Docketed: 10/2-1/01 Resp. to Rest. Req due 3/27/02 Final deadline
OCT 0 4 2001
UTXC:664
DLP
LM

Office Action Summary	Application No.	Applicant(s)	
	09/599,152	YANG ET AL.	
	Examiner	Art Unit	
	D. L. Jones	1619	

OIPE IAP86 SEP 06 2005 PATENT & TRADEMARK OFFICE

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-51 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-51 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESTRICTION INTO GROUPS

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1-32, drawn to composition and kit wherein the composition comprises a radionuclide, ethylene cysteine, and a tissue specific ligand, classified in class 424, subclass 1.65.

   II. Claims 33-41, drawn to a method of synthesizing ethylene dicysteine for imaging and a method of labeling for imaging purposes, classified in class 424, subclass 9.1.

   III. Claims 42-50, drawn to a reagent and kit comprising a ligand linked to a Tc-99m moiety, classified in class 534, subclass 14.

   IV. Claim 51, drawn to a method of determining the effectiveness of a drug candidate for tumor, classified in class 424, subclass 9.2.

2. The inventions are distinct, each for the other because of the following reasons:

Inventions (I and II), (II and II), and (I and IV) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the .product may be used to image a tumor or infection or as a means of determining whether a potential drug is effective against a tumor.

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

ELECTION OF SPECIES

4. Claims 1-51 are generic to a plurality of disclosed patentably distinct species comprising ethylenedicysteine drug conjugates. In particular, the conjugates comprise a radionuclide, ethylenedicystiene, and a tissue specific ligand. Possible tissue specific ligands include an anticancer agent, DNA topisomerase inhibitor, antimetabolite, tumor marker, folate receptor targeting ligand, tumor apoptotic cell targeting ligand, tumor hypoxia targeting ligand, DNA intercalator, receptor marker, peptide, nucleotide, organ specific ligand, antibiotic, antifungal, antibody, glutamate pentapeptide, or an agent that mimics glucose. Possible radionuclides include Tc-99m, Re-186, Re-188, Sm-183, Ho-166, Y-90, Sr-89, Ga-67, Ga-68, In-111, Gd-183, Fe-59, Ac-225, Bi-212, At-211, Cu-64, and Cu-62. Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed.

Note: Applicant is respectfully requested to elect a radionuclide and a *specific* tissue specific ligand within the elected group above for examination.

5. Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the

case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

6. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

7. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (703) 308-4640. The examiner can normally be reached on Mon.-Fri. (alternate Mon.), 6:45 a.m. - 4:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Diana Dudash can be reached on (703) 308- 2328. The fax phone numbers for the organization where this application or proceeding is assigned are (703)

308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

D. L. Jones
Primary Examiner
Art Unit 1619

September 24, 2001

OIPE MAP86 SEP 0 6 2005 PATENT & TRADEMARK OFFICE

Form PTO 948 (Rev. 6/01) U.S. DEPARTMENT OF COMMERCE - Patent and Trademark Office - Application No. 9/599,152

NOTICE OF DRAFTSPERSON'S PATENT DRAWING REVIEW

The drawing(s) filed (insert date) 6.21.00 are:

A. ☐ approved by the Draftsperson under 37 CFR 1.84 or 1.152.

B. ☑ objected to by the Draftsperson under 37 CFR 1.84 or 1.152 for the reasons indicated below. The Examiner will require submission of new, corrected drawings when necessary. Corrected drawing must be sumitted according to the instructions on the back of this notice.

1. DRAWINGS. 37 CFR 1.84(a): Acceptable categories of drawings: Black ink. Color.
   - ___ Color drawings are not acceptable until petiton is granted. Fig(s) _____
   - ___ Pencil and non black ink not permitted. Fig(s) _____
2. PHOTOGRAPHS. 37 CFR 1.84(b)
   - ___ 1 full-tone set is required. Fig(s) _____
   - ___ Photographs may not be mounted. 37 CFR 1.84(e)
   - ✓ Poor quality (half-tone). Fig(s) 11A-12, 14A-15D, 17-20B, 25, 26, 29-35, 37A, 81-86C
3. TYPE OF PAPER. 37 CFR 1.84(e)
   - ___ Paper not flexible, strong, white, and durable. Fig(s) _____
   - ✓ Erasures, alterations, overwritings, interlineations, folds, copy machine marks not accepted. Fig(s) 1-86C
   - ___ Mylar, velum paper is not acceptable (too thin). Fig(s) _____
4. SIZE OF PAPER. 37 CFR 1.84(f): Acceptable sizes:
   - ___ 21.0 cm by 29.7 cm (DIN size A4)
   - ___ 21.6 cm by 27.9 cm (8 1/2 x 11 inches)
   - ___ All drawing sheets not the same size. Sheet(s) _____
   - ___ Drawings sheets not an acceptable size. Fig(s) _____
5. MARGINS. 37 CFR 1.84(g): Acceptable margins:

   Top 2.5 cm Left 2.5cm Right 1.5 cm Bottom 1.0 cm SIZE: A4 Size

   Top 2.5 cm Left 2.5 cm Right 1.5 cm Bottom 1.0 cm SIZE: 8 1/2 x 11

   Margins not acceptable. Fig(s) 1, 7-11A, 12, 13, 18, 20A, 21-27, 29, 37A, 38A-48A, 55A-
   - ✓ Top (T) ✓ Left (L)
   - ✓ Right (R) ✓ Bottom (B)
6. VIEWS. 37 CFR 1.84(h)

   REMINDER: Specification may require revision to correspond to drawing changes.

   Partial views. 37 CFR 1.84(h)(2)
   - ___ Brackets needed to show figure as one entity. Fig(s) _____
   - ___ Views not labeled separately or properly. Fig(s) _____
   - ___ Enlarged view not labeled separetely or properly. Fig(s) _____
7. SECTIONAL VIEWS. 37 CFR 1.84 (h)(3)
   - ___ Hatching not indicated for sectional portions of an object. Fig(s) _____
   - ___ Sectional designation should be noted with Arabic or Roman numbers. Fig(s) _____
8. ARRANGEMENT OF VIEWS. 37 CFR 1.84(i)
   - ___ Words do not appear on a horizontal, left-to-right fashion when page is either upright or turned so that the top becomes the right side, except for graphs. Fig(s) _____
9. SCALE. 37 CFR 1.84(k)
   - ___ Scale not large enough to show mechanism without crowding when drawing is reduced in size to two-thirds in reproduction. Fig(s) _____
10. CHARACTER OF LINES, NUMBERS, & LETTERS. 37 CFR 1.84(i)
    - ✓ Lines, numbers & letters not uniformly thick and well defined, clean, durable, and black (poor line quality). Fig(s) 1-86C
11. SHADING. 37 CFR 1.84(m)
    - ___ Solid black areas pale. Fig(s) _____
    - ✓ Solid black shading not permitted. Fig(s) 48B
    - ___ Shade lines, pale, rough and blurred. Fig(s) _____
12. NUMBERS, LETTERS, & REFERENCE CHARACTERS. 37 CFR 1.84(p)
    - ✓ Numbers and reference characters not plain and legible. Fig(s) 1-86C
    - ✓ Figure legends are poor. Fig(s) 1-86C
    - ___ Numbers and reference characters not oriented in the same direction as the view. 37 CFR 1.84(p)(1) Fig(s) _____
    - ✓ English alphabet not used. 37 CFR 1.84(p)(2) Figs _____
    - ___ Numbers, letters and reference characters must be at least .32 cm (1/8 inch) in height. 37 CFR 1.84(p)(3) Fig(s) _____
13. LEAD LINES. 37 CFR 1.84(q)
    - ___ Lead lines cross each other. Fig(s) _____
    - ___ Lead lines missing. Fig(s) _____
14. NUMBERING OF SHEETS OF DRAWINGS. 37 CFR 1.84(t)
    - ___ Sheets not numbered consecutively, and in Arabic numerals beginning with number 1. Sheet(s) _____
15. NUMBERING OF VIEWS. 37 CFR 1.84(u)
    - ___ Views not numbered consecutively, and in Arabic numerals, beginning with number 1. Fig(s) _____
16. CORRECTIONS. 37 CFR 1.84(w)
    - ___ Corrections not made from prior PTO-948 dated _____
17. DESIGN DRAWINGS. 37 CFR 1.152
    - ___ Surface shading shown not appropriate. Fig(s) _____
    - ___ Solid black shading not used for color contrast. Fig(s) _____

COMMENTS

REVIEWER J. CHASE DATE 9.26.01 TELEPHONE NO. 703 305 8430

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EXHIBIT 2

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I hereby certify that this correspondence is being deposited with the U.S. Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231, on the date below:

10/26/01
Date

David L. Parker

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
Yang, et al.

Serial No.: 09/599,152

Filed: June 21, 2000

For: ETHYLENEDICYSTEINE (EC)-DRUG CONJUGATES, COMPOSITIONS AND METHODS FOR TISSUE SPECIFIC DISEASE IMAGING

Group Art Unit: 1645

Examiner: D. Jones

Atty. Dkt. No.: UTXC:664/DLP

RESPONSE TO RESTRICTION REQUIREMENT DATED SEPTEMBER 27, 2001

Commissioner for Patents
Washington, D.C. 20231

Commissioner:

This paper is submitted in response to the Restriction Requirement dated September 27, 2001 for which the date for response is October 27, 2001.

It is believed that no fee is due; however, should any fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to this document, the Commissioner is authorized to deduct said fees from Fulbright & Jaworski L.L.P. Account No.: 50-1212/10020527/DLP.

Please enter the following amendments and consider the accompanying remarks.

AMENDMENTS

Claims

Please cancel claims 1 and 42-51 without prejudice as directed to non-elected inventions.

Please amend claims 2-32 as set forth below:

2. The method of claim 33, wherein said tissue specific is conjugated to said ethylenedicysteine on both acid arms of the ethylenedicysteine.

3. The method of claim 33, wherein said radionuclide is ^{99m}Tc, ^{188}Re, ^{186}Re, ^{183}Sm, ^{166}Ho, ^{90}Y, ^{89}Sr, ^{67}Ga, ^{68}Ga, ^{111}In, ^{183}Gd, ^{59}Fe, ^{225}Ac, ^{212}Bi, ^{211}At, ^{64}Cu or ^{62}Cu.

4. The method of claim 3, wherein said radionuclide is ^{99m}Tc.

5. The method of claim 35, wherein said tissue specific ligand is an anticancer agent, DNA topoisomerase inhibitor, antimetabolite, tumor marker, folate receptor targeting ligand, tumor apoptotic cell targeting ligand, tumor hypoxia targeting ligand, DNA intercalator, receptor marker, peptide, nucleotide, organ specific ligand, antibiotic, antifungal, antibody, glutamate pentapeptide or an agent that mimics glucose.

6. The method of claim 5, wherein said tissue specific ligand is an anticancer agent.

7. The method of claim 6, wherein said anticancer agent may be selected from the group consisting of methotrexate, doxorubicin, tamoxifen, paclitaxel, topotecan, LHRH, mitomycin C, etoposide tomudex, podophyllotoxin, mitoxantrone, camptothecin, colchicine, endostatin, fludarabin, gemcitabine and tomudex.

8. The method of claim 5, wherein said tissue specific ligand is a tumor marker.

9. The method of claim 8, wherein said tumor marker is PSA, ER, PR, CA-125, CA-199, CEA AFP, interferons, BRCA1, HER-2/neu, cytoxan, p53, endostatin or a monoclonal antibody (e.g., antisense).

10. The method of claim 5, wherein the tissue specific ligand is a folate receptor targeting ligand.

11. The method of claim 10, wherein the folate receptor targeting ligand is folate, methotrexate or tomudex.

12. The method of claim 11, wherein the ligand derivative is ^{99m}Tc-EC-folate.

13. The method of claim 11, wherein the ligand derivative is ^{99m}Tc-EC-methotrexate.

14. The method of claim 11, wherein the ligand derivative is ^{99m}Tc-EC-tomudex.

15. The method of claim 5, wherein the tissue specific ligand is a tumor apoptotic cell targeting ligand or a tumor hypoxia targeting ligand.

16. The method of claim 15, wherein the tissue specific ligand is annexin V, colchicine, nitroimidazole, mitomycin or metronidazole.

17. The method of claim 16, wherein the ligand derivative is ^{99m}Tc-EC-annexin V.

18. The method of claim 16, wherein the ligand derivative is ^{99m}Tc-EC-colchicine.

19. The method of claim 16, wherein the ligand derivative is ^{99m}Tc-EC-nitroimidazole.

20. The method of claim 16, wherein the ligand derivative is ^{99m}TC-EC-metronidas.

21. The method of claim 5, wherein the tissue specific ligand is glutamate pentapeptide.

22. The method of claim 0, wherein the ligand derivative is 99mTc-EC-glutamate pentapeptide.

23. The method of claim 5, wherein the tissue specific ligand is an agent that mimics glucose.

24. The method of claim 23, wherein the agent that mimics glucose is neomycin, kanamycin, getnamycin, paromycin, amikacin, tobramycin, netilmicin, ribostamycin, sisomicin, micromicin, lividomycin, dibekacin, isepamicin, astromicin, or an aminoglycoside.

25. The method of claim 24, wherein the ligand derivative is 99mTc-EC-neomycin.

26. The method of claim 24, wherein the ligand derivative is 99mTc-EC-kanamycin.

27. The method of claim 24, wherein the ligand derivative is 99mTc-EC-aminoglycosides.

28. The method of claim 24, wherein the ligand derivative is 99mTc-EC-gentamycin.

29. The method of claim 24, wherein the ligand derivative is 99mTc-EC-tobramycin.

30. The method of claim 2, further comprising a linker conjugating EC to said tissue specific ligand.

31. The method of claim 30, wherein the linker is a water soluble peptide, glutamic acid, aspartic acid, bromo ethylacetate, ethylene diamine or lysine.

32. The method of claim 31, wherein the tissue specific ligand is estradiol, topotecan, paclitaxel, raloxifen, etoposide, doxorubricin, mitomycin C, endostatin, annexin V, LHRH, octreotide, VIP, methotrexate or folic acid.

REMARKS

Applicants here elect to proceed with the Group II invention, represented by claims 33-41. Applicant has further amended claims 2-32 of the Group I invention, to make them applicable to the Group II invention (by putting them into method claim format). Therefore, claims 2-41 are currently pending.

The Examiner is invited to contact the undersigned attorneyat (512) 536-3055 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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Date: 10/26/01

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CLAIMS AFTER RESPONSE TO RESTRICTION REQUIREMENT

2. The method of claim 33, wherein said tissue specific is conjugated to said ethylenedicysteine on both acid arms of the ethylenedicysteine.

3. The method of claim 33, wherein said radionuclide is ^{99m}Tc, ^{188}Re, ^{186}Re, ^{183}Sm, ^{166}Ho, ^{90}Y, ^{89}Sr, ^{67}Ga, ^{68}Ga, ^{111}In, ^{183}Gd, ^{59}Fe, ^{225}Ac, ^{212}Bi, ^{211}At, ^{64}Cu or ^{62}Cu.

4. The method of claim 3, wherein said radionuclide is ^{99m}Tc.

5. The method of claim 35, wherein said tissue specific ligand is an anticancer agent, DNA topoisomerase inhibitor, antimetabolite, tumor marker, folate receptor targeting ligand, tumor apoptotic cell targeting ligand, tumor hypoxia targeting ligand, DNA intercalator, receptor marker, peptide, nucleotide, organ specific ligand, antibiotic, antifungal, antibody, glutamate pentapeptide or an agent that mimics glucose.

6. The method of claim 5, wherein said tissue specific ligand is an anticancer agent.

7. The method of claim 6, wherein said anticancer agent may be selected from the group consisting of methotrexate, doxorubicin, tamoxifen, paclitaxel, topotecan, LHRH, mitomycin C, etoposide tomudex, podophyllotoxin, mitoxantrone, camptothecin, colchicine, endostatin, fludarabin, gemcitabine and tomudex.

8. The method of claim 5, wherein said tissue specific ligand is a tumor marker.

9. The method of claim 8, wherein said tumor marker is PSA, ER, PR, CA-125, CA-199, CEA AFP, interferons, BRCA1, HER-2/neu, cytoxan, p53, endostatin or a monoclonal antibody (e.g., antisense).

10. The method of claim 5, wherein the tissue specific ligand is a folate receptor targeting ligand.

11. The method of claim 10, wherein the folate receptor targeting ligand is folate, methotrexate or tomudex.

12. The method of claim 11, wherein the ligand derivative is ^{99m}Tc-EC-folate.

13. The method of claim 11, wherein the ligand derivative is ^{99m}Tc-EC-methotrexate.

14. The method of claim 11, wherein the ligand derivative is ^{99m}Tc-EC-tomudex.

15. The method of claim 5, wherein the tissue specific ligand is a tumor apoptotic cell targeting ligand or a tumor hypoxia targeting ligand.

16. The method of claim 15, wherein the tissue specific ligand is annexin V, colchicine, nitroimidazole, mitomycin or metronidazole.

17. The method of claim 16, wherein the ligand derivative is ^{99m}Tc-EC-annexin V.

18. The method of claim 16, wherein the ligand derivative is ^{99m}Tc-EC-colchicine.

19. The method of claim 16, wherein the ligand derivative is ^{99m}Tc-EC-nitroimidazole.

20. The method of claim 16, wherein the ligand derivative is ^{99m}TC-EC-metronidas.

21. The method of claim 5, wherein the tissue specific ligand is glutamate pentapeptide.

22. The method of claim 0, wherein the ligand derivative is 99mTc-EC-glutamate pentapeptide.

23. The method of claim 5, wherein the tissue specific ligand is an agent that mimics glucose.

24. The method of claim 23, wherein the agent that mimics glucose is neomycin, kanamycin, getnamycin, paromycin, amikacin, tobramycin, netilmicin, ribostamycin, sisomicin, micromicin, lividomycin, dibekacin, isepamicin, astromicin, or an aminoglycoside.

25. The method of claim 24, wherein the ligand derivative is 99mTc-EC-neomycin.

26. The method of claim 24, wherein the ligand derivative is 99mTc-EC-kanamycin.

27. The method of claim 24, wherein the ligand derivative is 99mTc-EC-aminoglycosides.

28. The method of claim 24, wherein the ligand derivative is 99mTc-EC-gentamycin.

29. The method of claim 24, wherein the ligand derivative is 99mTc-EC-tobramycin.

30. The method of claim 2, further comprising a linker conjugating EC to said tissue specific ligand.

31. The method of claim 30, wherein the linker is a water soluble peptide, glutamic acid, aspartic acid, bromo ethylacetate, ethylene diamine or lysine.

32. The method of claim 31, wherein the tissue specific ligand is estradiol, topotecan, paclitaxel, raloxifen, etoposide, doxorubricin, mitomycin C, endostatin, annexin V, LHRH, octreotide, VIP, methotrexate or folic acid.

33. A method of synthesizing a radiolabeled ethylenedicysteine derivative for imaging comprising the steps:

a) obtaining a tissue specific ligand;

b) admixing said ligand with ethylenedicysteine (EC) to obtain an EC-tissue specific ligand derivative; and

c) admixing said EC-tissue specific ligand derivative with a radionuclide and a reducing agent to obtain a radionuclide labeled EC-tissue specific ligand derivative, wherein the EC forms an N_2S_2 chelate with the radionuclide.

34. The method of claim 33, wherein said reducing agent is a dithionite ion, a stannous ion or a ferrous ion.

35. A method for labeling a tissue specific ligand for imaging, comprising the steps:

a) obtaining a tissue specific ligand;

b) admixing the tissue specific ligand with ethylenedicysteine (EC) to obtain an EC-ligand drug conjugate; and

c) reacting the drug conjugate with ^{99m}Tc in the presence of a reducing agent to form an N_2S_2 chelate between the ethylenedicysteine (with or without linker) and the ^{99m}Tc.

36. The method of claim 35, wherein the tissue specific ligand is an anticancer agent, DNA topoisomerase inhibitor, antimetabolite, tumor marker, folate receptor targeting ligand, tumor apoptotic cell targeting ligand, tumor hypoxia targeting ligand, DNA intercalator, receptor marker, peptide, organ specific ligand, antibiotic, antifungal, glutamate pentapeptide or an agent that mimics glucose.

37. The method of claim 36, wherein the reducing agent is a dithionite ion, a stannous ion or a ferrous ion.

38. A method of imaging a site within a mammalian body comprising the steps of administering an effective diagnostic amount of a composition comprising a 99mTc labeled ethylenedicysteine-tissue specific ligand conjugate and detecting a radioactive signal from the ^{99m}Tc localized at the site.

39. The method of claim 38, wherein the site is a tumor.

40. The method of claim 38, wherein the site is an infection.

41. The method of claim 38, wherein the site is breast cancer, ovarian cancer, prostate cancer, endometrium, heart, lung, brain, liver, folate (+) cancer, ER (+) cancer, spleen, pancreas, or intestine.

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CLAIM AMENDMENTS: RESPONSE TO RESTRICTION REQUIREMENT

~~A composition for imaging comprising:~~

~~a radionuclide label;~~

~~ethylenedicysteine; and~~

~~a tissue specific ligand conjugated to said ethylenedicysteine;~~

~~wherein said ethylenedicysteine forms an N_2S_2 chelate with said radionuclide label.~~

2. The method ~~composition~~ of claim 33~~1~~, wherein said tissue specific is ~~ligand may be~~ conjugated to said ethylenedicysteine on ~~one or~~ both acid arms of the ethylenedicysteine.

3. The method ~~composition~~ of claim 33~~1~~, wherein said radionuclide is ^{99m}Tc, ^{188}Re, ^{186}Re, ^{183}Sm, ^{166}Ho, ^{90}Y, ^{89}Sr, ^{67}Ga, ^{68}Ga, ^{111}In, ^{183}Gd, ^{59}Fe, ^{225}Ac, ^{212}Bi, ^{211}At, ^{64}Cu or ^{62}Cu.

4. The method ~~composition~~ of claim 3, wherein said radionuclide is ^{99m}Tc.

5. The method ~~composition~~ of claim 35~~1~~, wherein said tissue specific ligand is an anticancer agent, DNA topoisomerase inhibitor, antimetabolite, tumor marker, folate receptor targeting ligand, tumor apoptotic cell targeting ligand, tumor hypoxia targeting ligand, DNA intercalator, receptor marker, peptide, nucleotide, organ specific ligand, antibiotic, antifungal, antibody, glutamate pentapeptide or an agent that mimics glucose.

6. The method ~~composition~~ of claim 5, wherein said tissue specific ligand is an anticancer agent.

7. The method ~~composition~~ of claim 6, wherein said anticancer agent may be selected from the group consisting of methotrexate, doxorubicin, tamoxifen, paclitaxel, topotecan, LHRH, mitomycin C, etoposide tomudex, podophyllotoxin, mitoxantrone, camptothecin, colchicine, endostatin, fludarabin, gemcitabine and tomudex.

8. The method ~~composition~~ of claim 5, wherein said tissue specific ligand is a tumor marker.

9. The method ~~composition~~ of claim 8, wherein said tumor marker is PSA, ER, PR, CA-125, CA-199, CEA AFP, interferons, BRCA1, HER-2/neu, cytoxan, p53, endostatin or a monoclonal antibody (e.g., antisense).

10. The method ~~composition~~ of claim 5, wherein the tissue specific ligand is a folate receptor targeting ligand.

11. The method ~~composition~~ of claim 10, wherein the folate receptor targeting ligand is folate, methotrexate or tomudex.

12. The method ~~composition~~ of claim 11, wherein the ligand derivative is ~~further defined as~~ ^{99m}Tc-EC-folate.

13. The method ~~composition~~ of claim 11, wherein the ligand derivative is ~~further defined as~~ ^{99m}Tc-EC-methotrexate.

14. The method ~~composition~~ of claim 11, wherein the ligand derivative is ~~further defined as~~ ^{99m}Tc-EC-tomudex.

15. The method ~~composition~~ of claim 5, wherein the tissue specific ligand is a tumor apoptotic cell targeting ligand or a tumor hypoxia targeting ligand.

16. The method ~~composition~~ of claim 15, wherein the tissue specific ligand is annexin V, colchicine, nitroimidazole, mitomycin or metronidazole.

17. The method ~~composition~~ of claim 16, wherein the ligand derivative is ~~further defined as~~ ^{99m}Tc-EC-annexin V.

18. The method ~~composition~~ of claim 16, wherein the ligand derivative is ~~further defined as~~ ^{99m}Tc-EC-colchicine.

19. The method ~~composition~~ of claim 16, wherein the ligand derivative is ~~further defined as~~ ^{99m}Tc-EC-nitroimidazole.

20. The method ~~composition~~ of claim 16, wherein the ligand derivative is ~~further defined as~~ ^{99m}TC-EC-metronidas.

21. The method ~~composition~~ of claim 5, wherein the tissue specific ligand is glutamate pentapeptide ~~(molecular weight 750-15,000)~~.

22. The method ~~composition~~ of claim 0, wherein the ligand derivative is ~~further defined as~~ 99mTc-EC-glutamate pentapeptide.

23. The method ~~composition~~ of claim 5, wherein the tissue specific ligand is an agent that mimics glucose.

24. The method ~~composition~~ of claim 23, wherein the agent that mimics glucose is neomycin, kanamycin, getnamycin, paromycin, amikacin, tobramycin, netilmicin, ribostamycin, sisomicin, micromicin, lividomycin, dibekacin, isepamicin, astromicin, or an aminoglycoside.

25. The method ~~composition~~ of claim 24, wherein the ligand derivative is ~~further defined as~~ 99mTc-EC-neomycin.

26. The method ~~composition~~ of claim 24, wherein the ligand derivative is ~~further defined as~~ 99mTc-EC-kanamycin.

27. The method ~~composition~~ of claim 24, wherein the ligand derivative is ~~further defined as~~ 99mTc-EC-aminoglycosides.

28. The method ~~composition~~ of claim 24, wherein the ligand derivative is ~~further defined as~~ 99mTc-EC-gentamycin.

29. The method ~~composition~~ of claim 24, wherein the ligand derivative is ~~further defined as~~ 99mTc-EC-tobramycin.

30. The method ~~composition~~ of claim 2, further comprising a linker conjugating EC to said tissue specific ligand.

31. The method ~~composition~~ of claim 30, wherein the linker is a water soluble peptide, glutamic acid, aspartic acid, bromo ethylacetate, ethylene diamine or lysine.

32. The method ~~composition~~ of claim 31, wherein the tissue specific ligand is estradiol, topotecan, paclitaxel, raloxifen, etoposide, doxorubricin, mitomycin C, endostatin, annexin V, LHRH, octreotide, VIP, methotrexate or folic acid.

33. A method of synthesizing a radiolabeled ethylenedicysteine derivative for imaging comprising the steps:

a) obtaining a tissue specific ligand;

b) admixing said ligand with ethylenedicysteine (EC) to obtain an EC-tissue specific ligand derivative; and

c) admixing said EC-tissue specific ligand derivative with a radionuclide and a reducing agent to obtain a radionuclide labeled EC-tissue specific ligand derivative, wherein the EC forms an N_2S_2 chelate with the radionuclide.

34. The method of claim 33, wherein said reducing agent is a dithionite ion, a stannous ion or a ferrous ion.

35. A method for labeling a tissue specific ligand for imaging, comprising the steps:

a) obtaining a tissue specific ligand;

b) admixing the tissue specific ligand with ethylenedicysteine (EC) to obtain an EC-ligand drug conjugate; and

c) reacting the drug conjugate with ^{99m}Tc in the presence of a reducing agent to form an N_2S_2 chelate between the ethylenedicysteine (with or without linker) and the ^{99m}Tc.

36. The method of claim 35, wherein the tissue specific ligand is an anticancer agent, DNA topoisomerase inhibitor, antimetabolite, tumor marker, folate receptor targeting ligand, tumor apoptotic cell targeting ligand, tumor hypoxia targeting ligand, DNA intercalator, receptor marker, peptide, organ specific ligand, antibiotic, antifungal, glutamate pentapeptide or an agent that mimics glucose.

37. The method of claim 36, wherein the reducing agent is a dithionite ion, a stannous ion or a ferrous ion.

38. A method of imaging a site within a mammalian body comprising the steps of administering an effective diagnostic amount of a composition comprising a 99mTc labeled ethylenedicysteine-tissue specific ligand conjugate and detecting a radioactive signal from the ^{99m}Tc localized at the site.

39. The method of claim 38, wherein the site is a tumor.

40. The method of claim 38, wherein the site is an infection.

41. The method of claim 38, wherein the site is breast cancer, ovarian cancer, prostate cancer, endometrium, heart, lung, brain, liver, folate (+) cancer, ER (+) cancer, spleen, pancreas, or intestine.

~~42. A kit for preparing a radiopharmaceutical preparation, said kit comprising a sealed container including a predetermined quantity of an ethylenedicysteine-tissue specific ligand~~

conjugate composition and a sufficient amount of reducing agent to label the conjugate with ^{99m}Tc.

43. The kit of claim 42, wherein the ethylenedicysteine-tissue specific ligand conjugate composition further comprises a linker between the ethylenedicysteine and the tissue specific ligand.

44. The kit of claim 42, wherein the tissue specific ligand is an anticancer agent, DNA topoisomerase inhibitor, antimetabolite, tumor marker, folate receptor targeting ligand, tumor apoptotic cell targeting ligand, tumor hypoxia targeting ligand, DNA intercalator, receptor marker, peptide, organ ligand, antibiotic, antifungal, glutamate pentapeptide or an agent that mimics glucose.

45. The kit of claim 43, wherein the tissue specific ligand is estradiol, topotecan, paclitaxel, raloxifen, etoposide, doxorubricin, mitomycin C, endostatin, annexin V, LHRH, octreotide, VIP, methotrexate or folic acid.

46. The kit of claim 45, wherein the linker is a water soluble peptide, glutamic acid, polyglutamic acid, aspartic acid, polyaspartic acid, bromoethylacetate, ethylenediamine or lysine.

47. A reagent for preparing a scintigraphic imaging agent comprising a tissue specific ligand covalently linked to a ^{99m}Tc binding moiety.

48. The reagent of claim 47, wherein the ^{99m}Tc binding moiety is ethylenedicysteine.

49. The reagent of claim 48, wherein the tissue specific ligand is an anticancer agent, DNA topoisomerase inhibitor, antimetabolite, tumor marker, folate receptor targeting ligand, tumor apoptotic cell targeting ligand, tumor hypoxia targeting ligand, DNA intercalator, receptor marker, peptide, organ specific ligand, antibiotic, antifungal, glutamate pentapeptide or an agent that mimics glucose.

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~~50. The reagent of claim 48, further comprising a linker between said tissue specific ligand and said ^{99m}Tc binding moiety.~~

~~51. A method of determining effectiveness of a candidate drug on a tumor, said method comprising:~~

~~a) obtaining a candidate drug;~~

~~b) conjugating said candidate drug with ethylenedicysteine (EC) to produce an EC-candidate drug conjugate;~~

~~c) chelating said candidate drug conjugate with ^{99m}Tc to produce a ^{99m}Tc-EC-candidate drug conjugate;~~

~~d) introducing said ^{99m}Tc-EC-candidate drug conjugate into a patient with a tumor; and~~

~~e) imaging said patient to determine the effectiveness of the candidate drug against the tumor.~~

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